UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

SANOFI, et al.,	:	Trial Volume 3
	:	CA NO. 14-264-RGA,
Plaintiffs,	:	12-265-RGA,
	:	14-292-RGA,
v.	:	14-1434-RGA
	:	
GLENMARK PHARMACEUTICALS	:	June 9, 2016
INC., et al	:	
	:	3:01 O'clock p.m.
Defendants,	:	

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TRANSCRIPT OF CLOSING ARGUMENTS

BEFORE THE HONORABLE RICHARD G. ANDREWS

UNITED STATES DISTRICT JUDGE

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P R O C E E D I N G S

THE COURT: Please be seated

Let me just say before we start, I would especially encourage everyone to speak relatively slowly, because it will try and help me. If you speak like you have your remarks written down, and you're just reading to me, I can't think as fast as you can read.

So, if you left a few things unsaid because of that, I doubt that it will be very important things.

Okay. So, Mr. Solander.

MR. SOLANDER: Good afternoon, your Honor.

I'd like to start with the issue of infringement, which is our burden by a preponderance of the evidence.

First of all, there is no dispute on the issue of direct infringement. There is no question that when their product is sold to the public, that 80 percent of time the doctors will prescribe it in a manner consistent with the patent claims.

THE COURT: So you say that -- I'm sorry -- this is actually closing arguments.

Never doctor. Go ahead.

MR. SOLANDER: Okay. So direct infringement is one of the elements of induced infringement and contributory infringement.

So just to make our infringement case a little clearer, I just wanted to simplify the claims and a label, if you would.

So imagine I have a claim to a method of preventing the hospitalization for -- a cardiovascular hospitalization in men. So very similar to what we have, but it would just be men.

And my label says it's indicated for the reduction of hospitalization. It doesn't say men or women.

There is really no question that that would be encouraging the prescription of that medication to men, okay?

What their argument basically is, is that in order for there to be infringement in that particular situation, the label has to say either, don't give it to woman, or give it only to men.

But that isn't the law, your Honor.

And that's -- the case that we cite for that proposition is the AstraZeneca case, which says, basically, induced infringement can be proven where the instructions in a proposed label would lead inevitably -- would inevitably lead some consumers to practice the claimed method. That is exactly what would happen in that particular situation.

And just to sort of point out the absurdity of their argument, imagine I had a Claim 2, which was the same as the first one, but directed to women.

And under their theory, even though that's the entire universe of people, they would not infringe the private claim of

that patent. And we don't think that's proper.

The original scenario is exactly what we have in this situation. We have a method for reducing the risk of hospitalization in a certain class of patients.

Now, the label says, method of reducing hospitalization. 80 percent of the time, it's used in that particular class of patients. It's only been proven to work in that particular class of patients. And the indication, itself, says, go look at the clinical studies where you find out that exact thing. And that is, it's only be proven to work in that class of patients.

So let me change the claim a little bit to mention the diuretics claim, which I know your Honor heard this week. And I want to make it clear that we're asserting those claims. Those are not afterthoughts.

So that -- this would be my first scenario, except it's a man with brown hair. So men with brown hair.

The label has this very same indication, but the clinical study section says, it's been shown to only work in men. And it is been shown to work well in men of all hair color.

That is exactly what we have in the significance with the diuretics. It works in this particular class of patients and it works contrary to the belief in the art in patients taking diuretics.

So they say there is no infringement, because there is no encouragement here. No encouragement to do things.

So just imagine, if I'm a doctor, and a patient -- a woman comes to me and she has Afib, she has hypertension, she has diuretics, she's been in the hospital a few times and once stop was overnight.

So I ask myself, should I prescribe Multaq?

So I have the label here. I look at the indication. It says, okay, it's indicated for the -- reduce the risk of hospitalization for atrial fibrillation in patients in sinus rhythm with a history of paroxysmal or persistent AF.

That's my patient.

And it says, oh, go to 14.

And Section 14 is the clinical section. And in the very first section there is ATHENA, and it says that this has been shown it keep people out of the hospital who are -- who have Afib and who have hypertension and are on a diuretic.

That is exactly the type of patient that I have here.

So I'm encouraged to prescribe her -- I'm certainly not discouraged to prescribe it to her.

Just a moment on contributory infringement.

Your Honor, the issue on contributory infringement is whether there is a non-infringing use. And that's the 20 percent they point to that is prescribed off label.

The law is quite clear on this. And we'll make it --

we'll cite these in our briefs. There are a number of cases.

But off-label uses of FDA-approved drugs are not non -- substantial non-infringing uses. And that is the Eli Lilly case at 435Fd. Appendix 917 and there's a number of District Court cases that I have that follow that.

So you don't get yourself out of contributory infringement just because some doctors prescribed the drug off label.

Let me turn, if I can, to anticipation.

And if I can have a slide up, please?

This is Zusman Demo 16.

This is the slide that Dr. Zusman took us through for anticipation. And I'm just going to focus on -- with the morning and evening meal and see what he has written next to it.

He has next to it the title and design of ATHENA. This is one of the documents. This also Hohnloser 2008.

Let me start with the clinicaltrials.gov. The first one.

So if I can have DTX 15?

So in his chart he says this can be found -- this particular element with the morning and evening meal can be found in the title, which doesn't mention food or meal at all, or in the detailed description. And the only thing in the detailed description that he pointed to was the 400 mgs BID.

The same thing is true of JTX 35. The other document

that they rely on for anticipation. Again, they point to the title at the very top of where it says 400 mgs BID.

And then they go to the second page where the design of ATHENA, and they point to the 400 milligrams BID.

Your Honor, I think the testimony was quite clear. BID simply means twice a day. It doesn't mean you take it with or without a meal.

Now, Dr. Zusman said, I would think that a POSA would interpret that in taking that with a meal. But that would be -- imagine Dr. Zusman writing prescriptions for Multaq that has to be taken with a meal, pursuant to the ATHENA study and its approval.

Just writing BID and assuming everybody knows that means with a meal, that would be very dangerous to patients, because they might take it without a meal and effectively skip a dose.

And we know that other AADs -- this is from Dr. Reiffel's presentation -- say, BID, and also have instructions as to how to take it either with or without a morning meal.

BID simply doesn't mean with food. There is no evidence, let alone clear and convincing evidence of that.

Moving quickly to the Public Use argument, your Honor.

We'll deal with all the elements of this defense in our brief, but I just want to point out one, which we think is dispositive.

And that is, it requires clear and convincing evidence of a public use in the United States. And we asked Dr. Zusman about this.

So if I could have transcript 332, 16 to 3335.

"So in terms of your opinion that was there a public use, you haven't identified a single patient that was treated in the United States according to Claim 1."

He said "No, I wasn't asked to do that."

3358 to 33517.

"And you certainly haven't identified a single patient that falls within the claim of the '167 patent?"

Again, he says, "No, I haven't."

So we believe, your Honor, that there's a failure of proof on the issue of public use. And we expect it will be dropped, but if not, we'll deal with the other issues that we don't think they have proven the other elements of the claim later.

So I'd like to turn to obviousness. And I want to do this a little bit of an unusual way to start with. It's a little bit of a role play, if you will.

So, if you'll indulge me, I want to imagine that we are in, you know, February of 2008, and I've gone down to the Patent Office to secure the claims that we ultimately have in this case, which is a -- which is a method of treatment with all the elements that we have.

And one thing is true. I don't yet have the results of ATHENA. I don't have them yet. It's February and they don't come out until March. I don't know what the results are.

So I'm representing my client. I'm a patent layer. I go to the Patent Office. I meet the examiner in person.

The first thing the examiner says to me is, well, we have to discuss the whole of the prior art. He says, you've got an interesting claim. It could be an invention. But we want to discuss the whole of the prior art.

I say, okay, well, let me start at the beginning.

He says, I don't know whole a lot about antiarrhythmic drugs, so why don't you start. Why don't you tell me about those.

Okay. Do let me tell you about a study that was done in the '90s. All the doctors out there were using antiarrhythmic drugs to prevent premature ventricular contractions. And they thought if we reduced PVCs, we reduce the life-threatening arrythmia that is associated with it. It sounds completely logical to me.

And they were giving those drugs and the NIH came in and said, wait a minute, how do we know that works?

Let's do a study. That was the Cast study. They did the study. It was stopped prematurely because they were killing more patients by giving them these drugs than might not.

And that was a sea change in the way that those drugs

were used.

So he says to me, he says, well, okay, less PVCs.

How about Afib?

All right.

Well, they did a similar thing in Afib. The conventional wisdom at the time was, you give a drug for atrial fibrillation, it stopped. It puts the person in sinus rhythm and that should lead to better cardiovascular outcomes.

Well, they did six trials over the years, which your Honor heard about. The Rate and Rhythm Trials in which they tried to prove just that.

And in every place in the rhythm control arms, the drug did what it was supposed to do. It put the patient in sinus rhythm. There was more sinus rhythm in those arms.

Unfortunately, all of those studies failed to show any benefit of a rhythm control drug. And, indeed, four out of the six showed more hospitalizations in that arm.

It led in to a sea change in the way doctors prescribed the drug.

The 2006 guidelines said, this might suggest that attempts restore sinus rhythm were presently available and antiarrhythmic drugs are obsolete.

These are the guidelines that cardiologists followed when they are treating patients.

And you'll recall that Dr. Reiffel, who was there at

the time said, my prescriptions dropped off, people stopped coming to me for these drugs. Another sea change.

So, the examiner said, okay, well, why don't you tell me a little bit about those drugs.

Okay. Well, let's talk about the other drugs.

All of them have problems, which I think is good for me. I am trying to get Dronedarone. All these other ones have problems. They have a pro-arrhythmias, they cause arrhythmias in some patients. They can be life-threatening. They have negative inotropism. They make the heart weaker, so it doesn't beat as strong. You have drug-drug interactions. They have conduction disorders. They interrupt the electrical signal in the heart. And they have organ toxicity. In particular, Amiodarone has organ toxicity.

Every year two out of every hundred patients that you are treating will have a life-threatening organ toxicity. And then two more the next year and two more the next year.

If you do it for ten years, with the same amount of patients, 20 of them will have that. You can't use it long-term.

He says, well, that sounds pretty bad.

Well, what about your drug? Your drug must be a good one?

No. Actually, we have all the same problems.

The drug was suspected that it could cause

pro-arrhythmias. I'll talk about that in a second. It could cause worsening heart failure. That's the finding in ANDROMEDA. It has adverse drug-drug interactions. You'll see that the EMEA says that. It has the sinus node dysfunction, which is the electrical conduit in the heart. And it has non-cardiac toxicities. So toxicities elsewhere in the body.

And, indeed, on the first one, the pro-arrhythmia, the type of pro-arrhythmia that you get -- and this is from the ANDROMEDA -- a paper after ANDROMEDA -- is Torsades de Pointes.

And this examiner -- I'd show you a picture of what that looks like, when the heart does that, but I think it would scare you. It looks like a screw, a chaotic screw.

So the examiner says, well, okay, it's got its side effects and it's got problems. Maybe it does what it's supposed to do really well.

I think, well, it has -- it has to two characteristics. It actually has a sinus rhythm, but it also has a rate control benefit.

Well, that's -- wait. Maybe we've got something to work with here.

How good a rate control drug is it?

Not that good. Not that good.

We did a study, EURIDIS and ADONIS, where we gave the drug against a placebo and it lowered the rate. But it didn't lower the rate enough to avoid a rate control drug. All these

people still needed to take a rate control drug to go low enough.

And the EMEA issued a report that said, no clinical benefit in terms of improvement in symptoms due to a fast heart rate. It couldn't exercise better than the patients that took the rate control.

So what about the sinus rhythm?

Maybe it's really good as a antiarrhythmic drug?

Not, not really, because it's actually -- it's antiarrhythmic properties are a modest rate. That's what was said after the -- the Dafne study.

Well, is it better than the other drug, even though it's somewhat modest?

No. In fact, it's the worst than all the drugs in terms of its efficacy in maintaining sinus rhythm. The worst one.

Well, I don't know how I'm going to give you a patent so far. You haven't shown me anything that impresses me.

How about safety? Is it safer than the other drugs?

Well, it just so happens we did a safety study called ANDROMEDA. And in ANDROMEDA we gave it to a relatively sick class of patients that are likely to be prescribed the drug when they get out there. They are going to have the same comorbidity, this heart failure.

Well, what happened in ANDROMEDA?

Well, we killed twice as many patients by giving them the drug than we did by giving them the placebo. And, so, it was stopped prematurely.

Okay, well, I don't know, did you go to the regulatory agencies and see what they think?

Yes. We submitted an application after we did the two studies to the regulatory agency.

Well, what did they say?

Oh, they turned us down. Both of them.

The EMEA said it wasn't safe enough. The F -- and, so, we withdrew it.

The FDA said the same thing. They said, we're not going to approve it unless you prove to us that it's safe.

Well, okay, does it have any benefits that might keep people out of the hospital any ways? How about palpitations?

No, not palpitations. You don't get admitted to the hospital for palpitations. So it might help the palpitations, but it's not going to keep out of hospital.

How about strokes?

No, no, not stroke. No antiarrhythmic drug has ever been shown to effective with a stroke. You have to take an coagulate drug along with it.

Okay, what about heart failure?

No, that was the problem in ANDROMEDA. Those patients had worsening heart failure and they're the ones that started

dying at a faster clip.

Okay, well, is there any evidence at all that you can give me, any evidence?

So far I'm not convinced that you deserve this patent for a reduction in risk of hospitalizations.

Well, yeah, I've got something. Let me show you a posthoc analysis. We went back into the data in EURIDIS and ADONIS, and we did the posthoc analysis, and we found in the green up there, that in the EURIDIS study, we reduced hospitalization or death to P value .02.

The examiner looks at this and says, well, this doesn't make any sense. In EURIDIS you have a shorter time to recurrence. The people went back into Afib faster than they did in ADONIS. Almost 60 days earlier.

And yet in EURIDIS you're claiming that you had a reduction in hospitalizations that was statistically significant.

And, by the way, ADONIS was not statistically significant.

Aren't they the same study?

Yes, they're the same study.

Should they be the same?

Yes, they should be the same.

Why aren't they?

A chance probably. I don't know. It doesn't make any

send to me either.

And, by the way, you're showing me hospitalizations or death. You're asking for a claim for cardiovascular hospitalization.

Yes, that's true, we don't have any data in cardiovascular hospitalizations by itself, but we do have cardiovascular hospitalization as a combined endpoint with death.

Okay, was that statistically significant?

No, that was not. .164. So we really don't if that was true.

Well, how about the hospitalizations you saw, the numbers?

Well, most of them were non-CV hospitalizations. So if you totaled them all up and you add 8.9, 5.8 of the 8.9 were non-CV hospitalizations.

Well, that doesn't make any sense to me.

How in the world do you teach somebody out of the hospital for a broken leg by giving them Multaq?

And it's interesting that the CV-hosp was even less than the Multaq. And, you know, doctors will tell you that that 3.1 percent is not even clinically meaningful. It means you have to treat 33 patients to get one with a benefit. And it wasn't statistically significant.

I'm just being honest. I have a duty of candor and let

me just continue.

The art at the time was saying, hey, be real careful of this posthoc analysis. People have written articles in the last year or so saying, be careful about the posthoc analysis. It has to be emphasized.

And everybody knows that posthoc analyses are not reliable predictors of what's going to happen in the future.

It's the Jancin article that I will show you. There is the Stein and there's the EMEA report.

Well, we've got a study going. I don't know what the results of it are yet, but it might show a benefit in cardiovascular hospitalizations.

Indeed, that's one of the endpoints of hypothesis we've got that effectively shows a benefit in cardiovascular hospitalization. We're going to prove that to be true or not.

Well, okay, that sounds good. I assume you're running it in the same study as you ran in the positive EURIDIS, and the same population as the EURIDIS and ADONIS study?

No, no, we're not doing that. The FDA wouldn't let us. They wanted a safety study after what happened in the ANDROMEDA.

They said, well, maybe the ANDROMEDA patients were too sick. You can exclude those, but we want you to use a still -- a relatively sick population.

So we picked the population that's close to AFFIRM. That's one of those six studies where the antiarrhythmic drugs

failed to produce better cardiovascular outcomes.

But that's the population we picked. And that population just so you know, is sicker. They're older. They've got more high blood pressure. They've got more structural heart disease. You've got more heart failure and you've got more of the NYHA Class III patients.

And everybody in the art was describing that as high-risk. These are high-risk patients.

Dr. Reiffel, who was on the stand, he said they're high-risk patients.

So all we've got is a protocol. We don't have any data. It's high-risk patients. We've got the posthoc data. We have given you the claim.

There is no examiner in the world that would give that claim without any evidence that it works, none, ever.

You have no evidence that it works. Nobody would consider giving that claim until the results of ATHENA study were in.

And for the same reason, none of that -- none of the evidence that you see -- all of the evidence that you see says that claim is valid. The ATHENA study was not superfluous or unnecessary.

So let me talk, your Honor, about the documents they did show you. We didn't see a lot about the prior art. I think Dr. Zusman spent about ten minutes on reasonable expectations of

success.

We saw a lot of other documents. We saw this one. This is the key document. I know your Honor said it fell in Sanofi's files. That may have actually been what happened. Nobody knows who wrote this document. It could have been a marketing person. We just don't know.

Dr. Radzik was shown it in his deposition. It came from his files, and said, I have no idea what this is.

The written subject information, this is the information given to the ATHENA patients.

And, your Honor -- first of all, we don't think they can establish this as prior art. We don't think they have.

But even assuming it is, if you look at it, it's the sentence that you asked Dr. Reiffel about. It also appeared in these studies that patients treated with Dronedarone were less frequently admitted to a hospital.

And Dr. Reiffel said, well, that it a posthoc analysis. And I guess if you believe a posthoc analysis, you believe it's true, but no POSA would believe posthoc analysis, as everybody else in the case has said.

And if you look at Dr. Zusman's institution, when they got this, they rewrote it.

If I could have JTX 218, the first page?

The purpose of the study, right there, is to find out if correcting atrial fibrillation could have an effect on the

risk or death for cardiovascular events.

We're going to find out.

And if you go to Page 539 at the bottom, the number 539.

It says, what is a placebo?

The effect of a placebo on the long-term outcome of your disease might be different. However, based on the currently-available information, there is no clear evidence that this will have a positive or negative difference.

When POSAs, cardiologists got a hold of this document, which was written for patients, not for POSAs, it doesn't matter what a patient is told in this case, it's how a POSA interprets it. They rewrote it to more accurately reflect that it's a hypothesis.

And that's exactly what Dr. Reiffel said his institution did.

He said, I wrote that instantly, as they were permitted to do.

If you look at the documents that we submitted to the FDA, you have Ms. Rurka took us to page -- this is JTX 47 -- she took us to the third page and pointed out a paragraph there.

But on the page before, the second page it says, this is the point. This is what she didn't show you.

A posthoc analysis was conducted. This is talking about the cardiovascular hospitalization in death one.

.164 is the P value. They told the FDA all about the posthoc nature of the result, and they told them that it wasn't statistically significant.

The very same thing is true in JTX 48. Another document that was submitted to the FDA as part of the package here. The very same paragraph that's in that document on Page 21.

That's what she showed you. That's what it says. The same thing. .164 posthoc analysis.

And let's talk about the transcript of Dr. Naccarelli. Remember Dr. Naccarelli. It's an interesting name.

I want to go to the page before the page that Ms. Rurka showed you. This is the on bottom of Line 51.

It says, if we go back to the EURIDIS and ADONIS trials, there's a posthoc analysis looking at the effect of the compound on death or cardiovascular hospitalization.

In blue he's talking about a slide he's got on Dronedarone. And in gray it's a placebo.

You can see there was a favorable trend that just nipped the physical significance, giving a signal generating a hypothesis for this drug. That's exactly what ATHENA study was designed to do.

If you go a little further on, on Page 241 of the transcript, the same document. You've got another cardiologist.

I guess I would preface my comments by saying, I think

any type of posthoc assessment of casualty is speculative, and I think that's important just to get on the table.

That's what those documents really say.

So let's talk about the Hohnloser statement. I'm checking my time here. The Hohnloser statement.

There's three ways one can consider that statement.

You can either say, I considered it based on -- let's consider that one first. I considered it based on as being reasonable.

And that's defendants are arguing. The doctors would just take it at face value and says there's a reasonable expectation, a statement of reasonable expectation of success.

But as you heard Dr. Zusman on cross-examination, cardiologists don't take things at face value.

He was shown the ANDROMEDA study. And it was taken to the hypothesis in the ANDROMEDA study -- and forgive me -- it stays, anticipating that Dronedarone would reduce the rate of hospitalization due to heart failure.

We asked him, what did you think of that at the time?

I absolutely disagreed with it.

He didn't take it at face value and say, oh, I think it's going to work. He said, I disagree with it.

And if you look at the other study, Pallas, Pallas had a similar statement in there about the hypothesis.

And he said -- Dr. Zusman said on the stand -- he

didn't believe that investigators have a reasonable expectation that Dronedarone would show a favorable benefit in that Pallas population. Now, Pallas was done after approval.

So I don't think any person of ordinary skill in the art, especially -- I mean, we're talking about cardiologists here who are evidentiary-based people, because they have been -- they have made mistakes in the past in the way they've prescribed drugs which have, frankly -- and, of course, they didn't intend to, but killed people.

So they want evidence. They don't take things at face value.

So the other conclusion you could read is that Dr. Hohnloser's statement is unreasonable. I don't think anybody is suggesting that. Dr. Hohnloser is a reputable scientist. He doesn't say things just -- he doesn't say crazy things.

So that leaves us with the third possibility.

He's stating the hypothesis for the ATHENA study. That's what he's doing. That's the proper I way to look at the statement. That's what a POSA would look at it, especially in view of all that prior art.

Now, Dr. Zusman relied on two documents in his obviousness analysis besides Hohnloser and clinicaltrials.gov. He had another two up there, but they aren't substantive.

One's a textbook that discusses EURIDIS and the other is a written consent form, which isn't prior art.

So look looking at those two documents, one of them is the EMEA document, which you remember was a report, a lengthy report, 30-something pages from the EMEA after Sanofi tried to get approval of this drug the first time.

And the EMEA pointed out a lot of things. It pointed out the drug interaction profile.

He said, there was no actively controlled studies that have been performed and the overall safety profile were concerns.

They said, the interaction profile of Dronedarone with other drugs is a problem.

Remember what Dr. Reiffel said.

If you have a drug-drug interaction, you've got to do one of two things.

You have to start all three the dose of the other drug so you avoid overdosing the person accidentally, or underdosing them accidentally, because of the interaction, or you've got to stop them from taking the drug. That is not good either, because they need those drugs.

So drug-drug interactions are bad.

He also said -- they looked at the EURIDIS and ADONIS study, too. And he said, the pools there do not show a significant effect in terms of rhythm control. Although, as we saw, that's quite modest, with atrial fibrillation and maybe atrial flutter.

But the clinical relevance needs further consideration.

In other words, if I control sinus rhythm, so what? What clinical benefit does that have for a patient other than system control for sinus rhythm?

To keep you out of the hospital or to keep you from having a stroke?

Who knows?

The only person in this courtroom that thought that if you control sinus rhythm, you control -- you can lead to better cardiovascular out comes automatically is Dr. Zusman.

In other words, Dr. Zusman's opinion is, if I control sinus rhythm, my patients will have better cardiovascular outcomes.

Drs. Kim and Reiffel both disagreed with that.

Dr. Reiffel is, frankly, one of the top of this field and has been for 40 years. And others have disagreed with him, too.

Dr. Falk, who I showed you in my opening disagreed with him. The authors of the New England Journal publication reporting the AFFIRM study disagreed with him. The authors of the Race study publication, also in the New England Journal of Medicine disagreed with him.

All of these people said, we thought that keeping the patient in sinus rhythm would lead to better cardiovascular outcomes. We did a study. We were wrong. These are Rate

versus Rhythm studies.

Dr. Dennis Roy, the lead investigator of the AF/CHF website. Dr. LaFuente-LaFuente -- that's a great name -- who published a review of the prior art in 2007, said that. And most importantly, the guide rules set forth for cardiologists to follow, which are written by the American College of Cardiology, the American Heart Association, the European Society of Cardiology and the Heart Rhythm Society -- that's what I read to you before -- attempts to suggest that it attempts to restore sinus rhythm with presently-available drugs are obsolete.

So the EMEA also mentioned sinus rhythm -- sorry -- the rate control aspect of the drug.

And it said, whether these findings can be considered as a surrogate for clinical benefit remains to be established.

In other words, we see it slows down the heart rate a little bit. We do not know if it actually improves anybody's clinical outcome. And we know that because it doesn't reduce it very much. It's modest.

And then they also mention the sinus rhythm.

They said, a reduction in time to death and hospitalization was noted -- I'm sorry. They also mentioned posthoc analysis. I missed one, a reduction in time to death and hospitalization is noted, but this reflects an ancillary analysis and needs further confirmation. In particular, in view of the negative effects seen in ANDROMEDA.

And they concluded that they could not approve the drug because the ratio between efficacy and safety has not been shown.

The other document that Dr. Zusman relied on is the Dale document.

There it said, ATHENA -- first of all, it recognized that ATHENA is a mortality study. ATHENA was designed as a safety, because ANDROMEDA had failed.

So it says, ATHENA was designed to evaluate the effect on Dronedarone on mortality. And it also, in the Dale article, also mentioned the worsening of heart failure and the failure of the ANDROMEDA study.

It then pointed out the risk of Torsades de Pointes, which is that terrible arrythmia a patient can get in some instances.

So what did they conclude in Dale?

This is the article that Dr. Zusman relies on.

They said, since their Dronedarone may increase mortality in patients with heart failure and it has not been extensively studied in other populations with structural heart disease, its use should be relegated to the treatment of atrial fibrillations in patients without structural heart disease.

Dale was telling the world -- telling the world, don't use in patients with structural heart disease.

Let's go to the ATHENA study and put up Table 2.

A POSA would know from this table that 60 percent of the people in the ATHENA study had a structural heart disease and it worked in those patients. It prevented cardiovascular hospitalization in those patients.

So even if you ignore all the rest of the prior art I've talked about, and only focus on the EMEA document, and the Dale document, there is no way you have would have a reasonable expectation of success that the ATHENA study would be positive.

Let me, if I can, just focus last on the posthoc analysis.

So if I can bring up JTX 170. This is the same article. This is the report on EURIDIS and ADONIS studies.

And Dr. Reiffel was taken to a page in the back. 995 was shown, this sentence, in addition, you know, in the posthoc analysis Dronedarone significantly reduced the rate of hospitalization and death -- or deaths -- excuse me.

And he was not taken to the data. But we've seen the data. Here it is.

So, again, I'm going to -- this data is the data that I'm summarizing or Dr. Reiffel summarized in his chart. I think it's easier to read that way.

So let's put it up.

So, again, the nominal P values -- those are not real P values, those are nominal P values, because they are posthoc. We had one where it was significant and the other where it was

not.

As I pointed out earlier, those make little sense in light of the time the first recurrence data that's shown to the left. Those should be reversed, if anything. If you believe Dr. Zusman at the time, the first recurrence has anything to do with hospitalization.

So, in addition, I explained this a little bit earlier. The data makes no sense when you look at the hospitalization data. It doesn't make any sense that Multaq would be helping with non-cardiovascular hospitalizations. It has no effect on that that anybody had ever identified. And those literally include things like if you go to the hospital for a broken arm.

So what's going on here?

And I just want -- I want to bring Dr. Thisted back into the room, if I can.

So what Dr. Thisted said was, the problems with posthoc analysis is that you are -- you do a lot of studies and that increases likelihood that the results are going to change. That's one thing.

He said, they are often selectively reported.

And he said, the data as often sub-optimal.

What do we know about these posthoc studies in this case?

You heard Dr. Bozzi. She was on the video tape. The young lady was the biostatistician in the case.

And she said -- and, your Honor, there was an issue with the transcript that I think is in the process being fixed, so I'm actually going to read from her transcript.

The court reporters have kindly agreed to fix this, but I'm reading it about Line 8 there.

She says -- she is talking about the adverse event reports, okay?

So these are reports that doctors fill out when something happens during the study, okay?

And one of the boxes they can tic is hospitalization. There's not a box for cardiovascular hospitalization.

Hospitalization. And they are asked if they could please to write in the reason for the hospitalization, okay?

And, so, that was the data that Sanofi went back and analyzed. So they gathered up all these adverse event forms and went through and made a judgment, as best they could, as to whether the doctor intended it to mean cardiovascular. Maybe he wrote MI, maybe he wrote stroke.

Okay. So that's probably a cardiovascular. Maybe in some instances it wasn't all that clear. Maybe he didn't write anything down.

Who knows?

There was no real requirement to do it, because it's not an endpoint in the study.

It wasn't pre-defined, okay?

So what does Dr. Bozzi say about that?

In the cases of a series of the event reports, there was a box, a mention of hospitalization is written, so we used this poor information.

That's what she means is, the information was not of high quality.

And we asked Dr. Zusman about this as well when he was on the stand.

"Question: In terms of the term hospitalization, first hospital for cardiovascular causes, a person of ordinary skill in the art wouldn't have known how many authors defined that term in the study."

He said, "That was not reported for EURIDIS and ADONIS. We don't know how they defined it. It was very specifically reported for ATHENA."

That's what Dr. Thisted was saying, you have a prespecified endpoint. You're super careful about how you define it, how you measure it, how you record it.

This is all done after the fact. Nobody was thinking ahead of time, oh, we better make sure that the doctors write down cardiovascular.

And yet we defined it for them and said be careful for it.

And he says -- and, so, the point is the term hospitalization for cardiovascular reasons could have a number

of different definitions you could use. It may have different definitions. So those doctors may not be recording it all the same. That's a quality of the data problem. So that's one of the things that Dr. Thisted talks about.

How about the number of analyses?

Dr. Radzik was on the video yesterday. He's the lead inventor of the case and worked on this project for 20 years.

And he says, it's data from a study?

Yes, we conducted hundreds of posthoc analysis.

Totally consistent with what Dr. Thisted said.

These companies do hundreds of them for the data package that goes to the FDA. It's not hard to do. This one may have taken some time, because they had to go through by hand through the adverse event reports, unless they happened to be computerized.

But often all it is, is telling the computer, look for this, look for this, look for this. You set them up, and run they run it, and it comes out very quickly. You can do hundreds of them.

And then doctor sits and explains you can do P values. That's what was done in this case. Hundreds of them. That's what Dr. Radzik is saying.

And Dr. Zusman again, we asked him, and there's really no way for a person of ordinary skill in the art to know how many posthoc analyses were done on the EURIDIS and ADONIS

studies?

He says, I don't have any means of knowing that. That's correct.

You wouldn't know it from Singh article. The Singh article, they only published the few that they published.

That's it. That's selective reporting. We know hundreds were done. We know that it was done on poor quality data. And we know that they selectively reported the ones that they were interested in.

That is exactly what Dr. Thisted was talking about.

I would like to end -- just if I can give an analogy to illustrate Dr. Thisted's point.

Let's assume I'm playing pool with somebody, and I have to make a shot that goes off one rail, off another rail, off another rail, another rail, hits the ball which then goes into the side pocket.

I ask somebody that is standing there and say, am I lucky or am I good?

And would it change your answer to that question if I told him in advance that I was going to do that exact shot.

That's pretty defined, okay?

Would you change your view of whether I'm lucky or good if I did it another time right in a row?

That's replication.

Now, let's say I was sitting at a bar and having a

glass of water, and somebody came up to me and said, that guy over there, I just saw him make that shot four times. What do you want to bet he can't do it a fifth time? I would take that bet. I'm betting that guy is a sharp hustler. He's got that trick shot down. There's no way I'm taking that bet. Never.

But what if another guy comes up and says, it took him 600 times to do that four shots. I probably would mortgage my house on that bet.

Your Honor, thank you.

THE COURT: Thank you, Mr. Solander.

In order to be fair to you, why don't we just take a short break, so I can go walk around some and come back.

Mr. Solander, you were great, but it's hard to just listen for an extended period of time?

(A break was held.)

(Court reconvened after the break.)

THE COURT: All right.

Please be seated. Ms. Rurka.

MS. RURKA: Your Honor, so I wanted to start by talking about the infringement case, because I think Mr. Solander did not state the correct standard to use for proving indirect infringement.

So let's start with the case law.

For inducement of infringement, the plaintiffs are required to prove that we had specific intent to induce

infringement, okay?

So it's their purchased. They have to show specific intent. It's not enough to show that we had knowledge of the infringing use. And it's not enough to show that we had -- that we knew that the acts were infringing. They have to show we intended for those acts to happen.

The only evidence they have, your Honor, is the label. That's it.

Dr. Kim did not talk to any doctors. He didn't cite any studies showing how doctors prescribe. He didn't talk to anybody people who would be using the defendants' drug. He can't, because our drugs are not on the market. All he has is the label.

The law is clear about what the label says and what it is required to say. And why that does not constitute inducement.

So they had to have direct evidence of intent and they don't have it. I mean, I'm sorry. They have to have evidence of intent, if they don't have direct evidence.

Then you've got to look at, is the circumstantial evidence enough to establish intent?

So first off, where a product has substantial non-infringing uses, intent cannot be inferred, even when there is knowledge, that some users of the products may be infringing the patent.

So when Mr. Solander said, that if you -- if the instructions say, give the drug, and your claim said, give the drug to men, then you're going to be giving the drug to men necessarily, that is the not enough to establish intent.

You have to have more. You have to have more evidence. There's an instruction to infringe the patent.

And there's absolutely, without question, substantial non-infringing uses.

Dr. Kim admitted -- all three, actually, cardiologists admitted that they prescribe this drug for patients without risk factors. And Dr. Kim admitted that that is a non-infringing use for the drug. It's useful. It's beneficial to their patients. And it is a non-infringing use of the drug.

So it's by definition a substantial non-infringing use under the case law. The use should have to be something other than frivolous for it to be a substantial non-infringing use.

So then we look at the label.

And what does the label say about how to use the drug?

The label says it's indicated to reduce the risk of hospitalization for atrial fibrillation in patients with persistent paroxysmal atrial fibrillation.

It does not say anything about the risk factors in the case section. Not one thing.

In that circumstance, you have to ask yourself, is this an instruction to use it only in the patients with the risk

factors.

And the testimony shows that, no, that is not an instruction.

Dr. Zusman said that this is what it means to him. Would a person of skill in the art think reading this indication and use instruction, that it would direct the drug to be administered to patients having cardiovascular risk factors.

It would not limit the use of the patients in any way other than those that are in sinus rhythm and have a history of major persistent atrial fibrillation.

Dr. Kim also stated, agreed. There is no explicit language in the label that says, do not prescribe to patients without the cardiovascular risk factors, right?

That's correct. There is no explicit language in here that tells you to do that and that's not enough to establish intent.

So what they do point to? Well, actually I'll just point out the statute or the regulation that applies here, requires in the indication section that you include for an indication only in selected sub-groups of the larger population, you must include a succinct description of the limitations of the usefulness of the drug and any uncertainty about anticipated clinical benefits, along with including a reference to the clinical studies section.

So you have to have all three; limitation, the

usefulness of the drug, uncertainty about anticipated clinical benefits, and cites to clinical studies.

And Dr. Kim agrees you need all three in order to instruct that that is limited to that sub-population.

That is not the case here.

And, actually, Dr. Kim agreed. There is no succinct description in the ATHENA population in the indication in the Multaq label, is there?

On a literal level, I agree with you, no, there is not there is no succinct description of any uncertainty about any clinical benefits in the Multaq label.

In my reading, it does not describe what the statement is saying. All it does is reference the clinical study section.

That is what they're tying their instruction to, your Honor, Footnote 14. This little note is what they say constitutes an instruction to infringe the patent.

You can see that they used to have the clinical risk factors here. The cardiovascular risk factors here. And they just took them out. And all they have is the citation to the clinical study section in Footnote 14.

That is not enough to show instruction on how to use the drug only in people with clinical risk -- with a clinical risk factor.

And here's what Section 14 looks like.

You have the clinical studies section here that

references five trials. It doesn't reference ATHENA only. It references all five.

And if you look at the 14, the 14 references the whole group of studies.

Dr. Kim testified, they say now that it was off-label use. It's off-label use based on the clinical studies section. It's off-label use to administer this drug to patients that don't have the risk factors.

That's not correct, your Honor.

Here EURIDIS and ADONIS are part of the clinical studies section. And Dr. Kim agreed the EURIDIS and ADONIS study is within the labeling claim. It's relevant data surrounding the anti-arrhythmic drug efficacy of the drug. It is relevant. It is part of the clinical development.

In addition, he said, those studies -- the patients in those studies, some of them included the risk factors, and some of them didn't.

So what you have here is just an ambiguous reference to 14 that references multiple clinical studies, some of which have patients that use -- that have the risk factors. Some of which do not.

And, in that case, you can't find intent to induce. It's not there. And there's case law directly on point.

I will point out -- and you've seen this before -- when they didn't want to reference the specific studies in the

warning section, they referenced specific studies.

14.3 is the ADONIS study. 14.4 is the Pallas study.

So there's nothing -- if they meant to exclude the risk factor patients only included the ATHENA patients, they should have said 14.1. That's not what their label says. Their label says all 14.

Here's the law, your Honor.

Where the instructions for use are neutral, like they are here, intent to induce cannot be inferred.

This United Therapeutics case, I actually have a copy of it here. This is a District of New Jersey case from 2014.

The law of inducement requires a showing by UTC -- the standards of the ANDA label -- actually instruct physicians to do -- to infringe the patent. Sandoz's label does not contain any explicit instruction.

And that's what Dr. Kim conceded on the stand.

The Court finds that the warnings in Sandoz's label do not amount to an implicit instruction. And in there the warning suggested that it could be used in an infringing manner.

So, basically, the label was neutral. There was a suggestion that it could be used in an infringing manner.

And the Court said that's not enough.

An instruction, a statement directing one to take some action, such as how to avoid a potential adverse event.

It's not enough to just say -- to instruct without

saying exactly how to infringe, you have to show some sort of intent that the product to be used that way. And it's not enough whether it label is neutral.

And here's a Federal Circuit case that's pretty close on point. This is the Vita-Mix case where there was accused blender. You've heard of Vita-Mix blenders. The blender gave specific directions within the product instruction manual, that to use the blender in a default position which could result in infringing uses.

And the Federal Circuit said, it may be lead to infringing uses, but there is no evidence of intent for users to do that.

And without the evidence of intent, again, where the instructions are neutral, you don't -- you can't find induced infringement.

So for that reason, we do not infringe the patent. And they have failed on their burden of proof on that.

Okay. So let's turn briefly to patent invalidity. And I'm going to focus on -- we do have a public use defense, your Honor. But I'm going to focus on a discussion mostly of obviousness, because I think that's where the big dispute is.

Mr. Solander spent a lot of time talking about drugs, anti-arrhythmic drugs, and I think Dr. Reiffel did on direct as well. And talked generally about what the state of the art looked like.

What they didn't talk much about was what was published and known specifically about Dronedarone. There were multiple clinical trials that took place before the patent application was filed. And there is no question that there was a lot of publication on this drug and on its stated ineffective efficacy prior to the filing date.

That was almost ignored by both Dr. Reiffel and Mr. Solander.

In particular, we talked, I think mostly at the trial about Hohnloser and clinicaltrials.gov. These are publications on the ATHENA clinical trials. And they are stipulated prior art.

So the question isn't, this is not a compound patent case, your Honor, this is a specific method, a very narrow specific method of use patent that is claimed here.

And the question is not, what did the world look like? Would a person be motivated to develop this drug?

That is not what we're talking about here.

We're talking about what was known about Dronedarone, and would a person of skill in the art expected to do what was expected to do what was claimed in the patent.

That is really the only dispute. There is no dispute that Hohnloser makes in clinicaltrials.gov disclosed every single limitation except for perhaps the minor side limitations, which are filled in by prior art.

There's no dispute that the main points of these claims are disclosed in those publications. None. There is not one word about a dispute about that.

If you want to talk about the side elements, there's two -- you know, Dr. Reiffel actually testified that he considers the only two elements missing to be administration in the fed state and the results of the clinical trial. That is it.

So administration, which is, do you give the drug with food and what are the results?

Everything. The method including, you know, reducing the risk of cardiovascular hospitalization is set forth in both of those documents.

So administration with food. I mean, this is not an issue, your Honor. Everybody admits the EMEA document that talks about the administration of Dronedarone says administer it with food.

It's not an issue of whether or not that's disclosed or whether or not you would be motivated to combine EMEA with the Hohnloser and clinicaltrials.gov document. It's not a dispute.

And then there's one claim that's a dependent claim that talks about diuretics again. It is not a dispute as to whether or not people would have known that some of those patients in the ATHENA trial were taking diuretics or specifically non-catching spira (ph)diuretics. It's just not a

dispute. Dr. Reiffel actually agreed with that at trial.

So the question is whether or not you believe that the method that was described in Hohnloser and clinicaltrials.gov would actually -- would reasonably expected to result.

The reduction in the risk of hospitalization, whether you reasonably expect that to result from the administration that was described in both of those publications.

And there is no question that you would, and that's what they told the world throughout this entire case -- throughout the entire timeline before the patent application was filed.

So here's kind of where we are.

At the time they were telling everybody, and other people were telling everybody that we expect this drug to work to reduce the risk of hospitalization. And we expect it based on what we've seen with this drug before.

The publication -- the studies that we've done with this drug, we expect this drug to work.

What they're trying to say now is, you shouldn't have believed us when we said that to the world, and you shouldn't believe everybody else that said that as well.

And that's just not right.

At the time, the relevant time frame is 2008. It's not now when Dr. Reiffel talked about how much he doubted that the drug would work. It's back in 2008.

What did the world look like?

And the world looked like this.

I'm going to get right to it.

First, it's not like it's far-fetched to think that if you treat the condition, you're getting to treat hospitalization for the condition. That's, you know, kind of a perquisite. If you are treating the condition, then you would expect that people aren't going to be hospitalized for it.

So that is kind of a basis for an expectation that it would work, but we have more than that in this case.

First, I want to address the standard for reasonable expectation of success.

This is Dr. Reiffel's belief on what the standard is.

"You're saying a person skilled in the art cannot expect success until they have placebo controlled Phase III clinical trials establishing that the drug works in that way, isn't is that right?

"Yes.

"That's your position?

"Yes.

"That's what reasonable expectation of success means to you?

"Yes."

Sure, you need Phase III placebo controlled clinical trials most of the time to get FDA approval, probable to get

EMEA approval as well for your drug to administer it to patients in the indicated way. That does not mean that you have to have that for reasonable expectation of success.

That's not the standard. The FDA standard for approval is not patentability standards. The standard for patentability is expectation of success need only be reasonable, not absolute.

The case law is clear, obviousness cannot be avoided simply by showing some degree of you unpredictability in the art, so long as there was a reasonable probability of success.

One skilled in the art would have a reasonable expectation of success at the time the invention was made and merely had to verify that expectation. That's the standard. It's not FDA approval of a drug.

All the discussion of posthoc analysis, your Honor -- posthoc, certainly the FDA does not necessarily allow you to get a label claim based on posthoc analysis. Sometimes they do. They actually did in this case allow that, but often they don't. They require it to be a primary outcome.

That's not what this standard -- that's not the standard that applies here, your Honor.

The standard that applies here is whether or not a person of skill in the art, being in the art at the time, would reasonably expect that it would be successful.

So -- and here's what they said -- here's what actually the world said at the time.

Sanofi provided a written subject information to be provided to patients. That written subject information described Dronedarone being used in the EURIDIS and ADONIS trial. Based on that knowledge, it is expected, that Dronedarone improves the outcome in atrial fibrillation and atrial-flutter patients by reducing the admissions to hospital and prolonging the time in normal heart rhythm.

So Mr. Solander showed you a page earlier on, that they are trying to prove that in this clinical trial. And based -- sure, that was the goal was to do the clinical trial, so they could get FDA approval for that.

They also told the patients what they expected to be the results of this clinical trial. It is expected that it would reduce the admissions to hospitals, which is exactly what the claim says.

We had this internal document from Sanofi. The finding about the posthoc analysis from the EURIDIS and ADONIS trials. It is key and constitutes the clinical basis for the expected benefit of Dronedarone in the ATHENA study.

So they were saying internally that they expected that the ATHENA study would result in what is in the method that is claimed.

They told the FDA that they thought the reduction in hospitalizations was going to be expected.

Given the trend for a beneficial effect of Dronedarone

in the AF/AFL population, derived from the EURIDIS and ADONIS trials, it is expected that treatment with Dronedarone can similarly decrease this combined endpoint of hospitalization for cardiovascular reasons, or any deaths, in high-risk patients with a history of AF/AFL.

They told the FDA this, because they wanted to be able to do the clinical trials. So, you know, they told the FDA the truth.

That's what they expected. Let us give this drug to patients in the ATHENA clinical trial.

In the clinical studies report they said, we designed that clinical trial in order to document what the expected benefit was they had told them in 2005 was expected.

And then when they went to the see the FDA, the ACOM meeting, the Advisory Committee meeting in order to ask the FDA for approval for Dronedarone.

Dronedarone has properties that can be expected to reduce the risk of death and cardiovascular hospitalization. And that was based on the posthoc analysis of EURIDIS and ADONIS. Other people in the art said they expected this.

Here's a New England Journal of Medicine reviewer who was commenting on the ATHENA paper that was going to be published.

In the present study, virtually all of the primary endpoint impact from Dronedarone was due to reduce

cardiovascular hospitalization for Afib recurrence.

This outcome is predictable based on well-documented ability of the Dronedarone to prevent AF recurrence.

In Hohnloser 2005, Dronedarone. In addition to its benefits for rate and rhythm control, reduced the combined endpoint of hospitalization or death in patients with AF.

Stein in 2005, in a posthoc analysis, Dronedarone significantly reduced the rate of hospitalization or death.

Jancin in 2006, the novel investigation of the anti-arrhythmic agent, Dronedarone, reduced by 27 percent the one-year combined incidence of hospitalization or death compared to placebo.

Singh in 2007, in a posthoc analysis, Dronedarone significantly reduced the rate of hospitalization or death.

And then we have Hohnloser again in January of 2008, after presenting the data related to EURIDIS and ADONIS said, since it was shown that Dronedarone is not only capable of maintaining sinus rhythm in many patients, but also of controlling heart rate in case of AFC lapses, it is expected that treatment with this compound will result in a significant reduction in the need of rehospitalizations for cardiovascular reasons.

So what the world looked like then is not anything like what Mr. Solander or Dr. Reiffel described on direct.

They described a world talking about drugs that have

nothing to do Dronedarone. That are not Dronedarone -- I should say -- they were drugs that were used to treat of ACH/AF. They weren't Dronedarone and there is dispute about that.

They had a list of multiple trials and multiple drugs. None of the trials or the drugs are about Dronedarone.

The studies, and the data, and the documents, and the publications on Dronedarone all pointed to this being an effective drug that could be used and was expected to be used to reduce cardiovascular hospitalizations.

So, you know, I showed you the slide at the opening and I will just kind of reiterate.

All the rate versus rhythm trials, so about the first half of Dr. Reiffel's testimony about rate versus rhythm trials, they were not about Dronedarone. They did not test Dronedarone. There was no comparison of Dronedarone to any other drug or the efficacy. They were -- they were about different drugs.

They actually showed that there was no significant difference in controlling rate versus controlling rhythm.

Dr. Reiffel admitted that on cross-examination that there was no significant difference. None of the -- as I said, none of the trials tested Dronedarone. And it's not disputed that Dronedarone was known to have both rate and rhythm controlling properties.

Now, would Dronedarone be used solely as a rate controlling drug?

No, but that doesn't mean it wasn't known to have the rate and rhythm controlling properties. It was. And that's not disputed.

And Dr. Zusman had testified about this in his direct.

I don't believe that the previous published or discussed rate versus rhythm trials would in any way discourage a person of ordinary skill in the art in understanding that Dronedarone would reduce the risk of hospitalization in patients participating in the ATHENA trial. And that's because people knew how the drug worked. And they knew it worked. And they had read all the publications saying how it worked and what they expected it to do.

A couple of other points.

The ANDROMEDA trial, I think there was a lot of discussion of the ANDROMEDA trial in Dr. Reiffel's testimony.

The reality is, everybody admitted that the drug -- the trial was not an Afib trial. The trial was a structural severe heart failure problem trial. And it was distinct. And actually Dr. Reiffel admitted that on cross that the patients from ANDROMEDA were far different than the patient -- the ANDROMEDA patients were far different from the ATHENA population, which was much closer to the EURIDIS and ADONIS patients.

So there is no reason to think that ANDROMEDA, the ANDROMEDA results would discourage someone from thinking that the drug would work. And, in fact, didn't discourage people.

It actually caused Sanofi to -- and the FDA allowed Sanofi to administer the drug to patients, to sick patients. So it didn't discourage anybody.

There is no evidence that anybody was discouraged at all about the ANDROMEDA trial, or the rate versus rhythm trials from testing this drug and putting the drug into humans.

And I would mention also, your Honor, there is a list of issues. There's a list of six drugs that Mr. Solander and Dr. Reiffel had put up on the screen and the problems with those drugs.

Those drugs were approved. The FDA approved them. And they still are and they're still on the market. Every drug presents issues with drug interactions.

I don't think there was evidence that Dronedarone had all of the issues that are listed there in the list, but the bottom line is, those drugs are approved and on the market, so is Dronedarone.

So there is no evidence that those characteristics of the drug would discourage someone from trying to develop the drug or get FDA approval for the drug. And it certainly didn't discourage Sanofi.

And, so, I just want to talk a little bit about secondary considerations, because I think actually, secondary considerations in this case confirm that the claims are obvious.

Here's why.

There's no doubt, and this is unrebutted testimony from Sanofi's only own witnesses that if they had gotten the okay from -- if Sanofi had gotten the okay from the FDA for the EURIDIS and ADONIS, they would have taken that indication. They would have taken the indication without the reduced risk of hospitalization. They would have taken the indication that it reduces of symptom of Afib. And they would have been perfectly happy with that.

And that's the testimony of Dr. Hamdani.

"If the FDA had, at this meeting, this July meeting said, yes, you may, based on the EURIDIS and ADONIS trials, would Sanofi have performed another safety clinical trial such as ATHENA?

"No, they would have accepted the AF reduction in the AF symptoms indication and moved on."

That's not what they claimed, your Honor. They claimed the reduce the risk of hospitalization.

Dr. Radzik, who was an inventor here, said, The ATHENA study was actually -- it was run to show that the drug was not deleterious or mortality, and this endpoint was just there. This is the hospitalization endpoint. Because you can't do a study just to show that a drug does not increase mortality. FDA required to them to put the reduced risk of hospitalization indication in or the endpoint in the ATHENA study. They didn't wanted to do it. They were asked to do it by FDA because the

FDA said, you can't use mortality as an endpoint."

So nobody believed at the time that there was anything inventive about reducing the risk of hospitalization. In fact, what they thought was, I would rather have the claim to Afib and move then to have to do this ATHENA study.

And that is what the -- the evidence showed.

What does that mean?

Actually, they marketed the drug based on reducing Afibs symptoms.

So these are Sanofi's marketing materials. And there is certainly marketing material related to reducing the risk of hospitalization. They actually marketed it to prolong time of first recurrence of Afib, reduce the symptomatic burden of Afib.

And Dr. Kim actually testified that that's true as well.

If they thought the reduced risk of hospitalization was a major indication and a breakthrough like they're saying now, then why are they marketing the drug to treat Afib by itself?

Because it's not a breakthrough. The reduced risk of hospitalization is not a breakthrough. And, in fact, what you see is, the drug plateaued as far as sales.

If the reduced risk of hospitalization was such a critical element to their claim, then why isn't their drug doing better in sales?

The bottom line is, the drug is fine. It's a good

drug. It treats patients with Afib. Doctors like to use it. They like to have it in their armament.

It's not a breakthrough and it's certainly not a breakthrough on the basis of a claim for reduced risk of hospitalization.

They didn't claim the compound itself. They didn't claim the drug for use in the atrial fibrillation.

They claimed a very specific use, reduced risk of hospitalization. And that use was fully expected based on what they had published in the art at the time.

So the claims are obvious and they don't have sufficient proof, your Honor, that we induced infringement of those claims.

I'd like to briefly address the '800 patent, the non-infringement issue of that still an open issue in the case.

And if you recall, your Honor, this was the patent claim -- the dispute was about pharmaceutically-acceptable, non-ionic hydrophilic surfactant, which you construed to mean, a surfactant which is not a polysorbate surfactant.

So the only issue here, your Honor, is you have to decide -- and we'll brief this, but I just wanted to preview it for you as well.

The only issue is whether this construction means that the entire composition must exclude polysorbates, or whether the composition can include polysorbates, as long as the composition

has another nonionic hydrophilic surfactant.

That's the nut of the issue for claim -- for interpreting your claim construction, your Honor.

Does the composition have to exclude polysorbates or can it include as long as there's something else in it, another surfactant in it? And this was your construction.

The '493 patent applicants amended the claims to explicitly exclude polysorbate surfactants in order to overcome a prior art rejection.

So what does that mean?

And that, by itself, might not give you enough context, but here's what it means.

This was the exclusion that the '493 patent claimant or the patent applicant did provided that the composition, the entire composition does not contain a polysorbate surfactant.

So that's what you -- that's -- the ruling was this phrase here in the '493 patent is what this term is supposed to be construed as.

The entire composition excludes the polysorbate surfactant.

Plaintiffs argued that we didn't make that argument in our briefs or at claim construction.

We absolutely did by insisting that the present invention is directed to poloxamers and amending the claims to exclude polysorbate surfactants, the applicants clearly stated

what their claimed invention is not, a formulation which contains a polysorbate surfactant.

What they said at the Markman Hearing, your Honor, the question is, does the language that is excluding polysorbates from the '493 patent, does that also apply to the '800 patent?

The language is, excluding it from the composition.

This is what they said during the '493 patent prosecution in order to disclaim polysorbates from the composition. Polysorbate surfactants are specifically excluded from the composition.

And then they amended their claims to exclude polysorbate surfactants from the composition.

Not from -- -not -- this was a flat-out exclusion from the composition. It wasn't a situation where you can have it as long as you had some other surfactant.

So what your Honor held -- actually, what happened was, they never reclaimed it in the '800 patent prosecution. They never clearly stated to the Patent Office, you have excluded this, and we want to reclaim it.

And what this Court did was say, I think that in order to properly recapture the disclaimed subject matter, the '800 applicants needed to clearly indicate their intent to do so. It is not enough that the examiner considered the surfactant. The examiner should have been made aware that polysorbate surfactants were previously excluded to overcome a rejection.

And they were excluded from the composition, your Honor. And that the applicants intended the new claim to recapture them. And that's why you adopted the claim construction that you did.

So we would ask for consideration of those facts and we'll brief it further in our post-trial briefing.

And with that, I'm finished.

THE COURT: All right.

Thank you, Ms. Rurka.

THE COURT: All right.

So let's just make sure that we have -- the parties, you talked about how much briefing you wanted?

MR. MINION: We have had some back and forth. Unfortunately, we weren't able to reach agreement.

THE COURT: All right.

Why don't you give me the goalpost and I will consider them.

MR. MINION: Our proposal, since we have the issue of infringement of invalidity, and then this claim construction, that there's an overall page limit that the parties are limited to for all issues that we can divide between opening, rebuttal, and reply.

THE COURT: Right. But presumably they are going to go first on invalidity and you're going to go first on infringement, right?

MR. MINION: Our problem with their proposal is, we

don't believe that we need that much space for infringement.

THE COURT: I don't think you do either.

I don't think the infringement period needs that much space.

MR. MINION: Right.

So we were trying to propose different -- different page limits for validity and from infringement. And they wanted them to be -- all of them to be 25, 25, 10.

MS. JOHNSON: Your Honor, that is what we proposed; 25 for each of the openings. The opening brief, which goes to invalidity, and 25 for the response brief.

On the non-infringement, we do have two patents to address in the non-infringement breach. The '167 patent and '800 patent. We think 25 pages for each of those briefs should be plenty sufficient.

THE COURT: You mean 25 pages? You don't mean three different 25 page briefs, do you?

MS. JOHNSON: No. I mean two 25 page briefs and then one 25 page reply brief.

THE COURT: So the infringement/non-infringement on the '167 patent, you know, I've been thinking that didn't require that much.

What do you think about the '800 patent claim construction?

MR. MINION: I think the proposal for -- that

defendants would proposed in terms of infringement is fine.

Our only request is that we'd like more than 25 pages for our rebuttal on invalidity.

THE COURT: Okay.

MR. MINION: That's our -- that's our only issue, your Honor.

THE COURT: How many pages would you like?

MR. MINION: 35.

MS. JOHNSON: And, your Honor, we don't think 35 pages is necessary. This has been a two-and-a-half day trial. We didn't spend that much time on invalidity, so I think 25 is enough on the opening brief on invalidity and the response.

THE COURT: All right.

So why don't we do this.

Since you agree that the non-infringement claim construction can be 25, 25, 10 --

MR. MINION: Yes.

THE COURT: -- so why don't we do that for the infringement and the claim construction.

For the invalidity, I'm not entirely sure that I don't think Mr. Minion is right, that 25 is enough on that, too.

But I'd rather -- but I think 30 -- I'll go with 30, 30, and 15, okay?

MR. MINION: Okay.

MS. JOHNSON: Okay.

THE COURT: All right.

So we have a -- we had dates as to when those were going to be due, right?

MR. MINION: That's correct, your Honor.

And I think that you had an order and then you added an extra day.

THE COURT: Right, I added an extra day. I'm not going to take it back now, even though I could.

But, so, it's based on tomorrow, right?

Because that's when we thought closing arguments were going to be. It is whatever it is.

In terms of providing a hyperlink briefs, when you're done with all of this, how much after the last brief is submitted do you need to do that?

MR. MINION: I think typically five days.

MS. JOHNSON: Five days is fine, your Honor.

THE COURT: Five business days or just five --

MR. MINION: Probably just five.

THE COURT: Remind me, what day of the week does this briefing end on?

MR. MINION: I don't remember.

MS. JOHNSON: I think it's due on Friday, July 1st.

THE COURT: July 1st. It's going to be a handicap.

So Friday, July 1st. So, actually, would it be unreasonable to say Friday, July 8th?

MS. JOHNSON: That's reasonable for us, your Honor.

MR. MINION: That's fine.

THE COURT: All right.

And the two little evidentiary issues that you were going to submit, I guess a one-page letter, and I guess now it's probably going to be a three-page letter, because you've got the Ardehali thing.

What I was thinking is, perhaps you could submit those more promptly, then maybe I can rule on them before you finish all this briefing.

MR. MINION: Your Honor, I think on the one evidentiary issue, now that we've had a chance to look at the statements that were in the FDA briefing document, we're comfortable foregoing it.

THE COURT: I'm sorry. So, in other words, you withdraw the objection?

MR. MINION: Yes.

THE COURT: Okay. And that leaves the Ardehali thing.

MR. MINION: Tuesday?

THE COURT: Okay. So --

MS. JOHNSON: We're back to one page?

THE COURT: Well, I think for that, because I really don't know what you're going to come up with, you had a lot of arguments the other day.

You know, why don't you see -- about how many pages

would you like?

MS. JOHNSON: One is fine for us, your Honor.

THE COURT: Okay. Well, Mr. Minion, one page is fine with --

MR. MINION: One page is fine with us, your Honor.

THE COURT: All right.

Well, I'm happy to do one. One page is fine.

So you're going to have -- when is it -- maybe you can get your one page in by Monday?

MS. JOHNSON: Monday? Wednesday.

MR. MINION: Wednesday.

THE COURT: Yes, Wednesday. And I think the two more pages, maybe I can -- if I recall my schedule for next week, maybe I can try to -- I'll get you something, maybe not by your first brief, but before you get to your second brief, okay?

MR. MINION: Thank you.

THE COURT: All right.

Is there anything else that we need to do.

MR. MINION: Nothing from us, your Honor.

MS. RURKA: Nothing from us, your Honor.

MR. SOLANDER: Excuse me. I just want to clarify something.

We go first on infringement.

Does that mean we go first on claim construction?

It's sort of their motion, but I'm willing to do it.

THE COURT: Well, so here's the thing.

I think you should go first, because I'm looking at that in the end as an infringement issue.

MR. SOLANDER: I get you.

THE COURT: One thing I would ask also.

Don't regard the issue here as being to try so much to tell me what you think I've already decided. I'm pretty sure, based on what I wrote and my memory, that I thought I was deciding something else, which was the construction of this phrase.

Maybe the analysis is not so different, but I would like you to approach it with -- I'm trying to get the right answer here, which may or may not be exactly what you think I said the last time around.

MR. SOLANDER: You won't be offended if we take that term a little de novo, just in terms of what we think you should do?

THE COURT: Yes, I will not be offended.

MR. SOLANDER. Okay, okay.

THE COURT: Okay?

All right. Is there anything else?

MR. SOLANDER: No, your Honor.

THE COURT: Well, thank you --

MR. SOLANDER: Thank you very much.

MS. RURKA: Thank you very much.

THE COURT: -- for presenting your cases very well and efficiently.

And I guess actually I would actually let the paralegal come forward. I will give you back the three volumes that I've accumulated in the meantime, somebody, or Mr. McArdle?

Sorry to be imposing on you here.

MR. MCARDLE: No problem, your Honor.

THE COURT: We'll be in recess. Thank you very much.

(The proceedings adjourned at 4:38 o'clock p.m.)

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